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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LOEB, BRONWEN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 03/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/976,687	HANSON	
	Examiner	Art Unit	
	Bronwen M. Loeb	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This action is in response to the amendment filed 3 January 2002 in which an amendment to the specification was submitted.

The as-filed claims has a numbering error. Specifically, claim numbers 21 and 22 were used twice. Starting with the second recitation of claim number 21, the claims were renumbered 23-41 under 37 CFR 1.126. The claim dependencies were accordingly corrected.

Claims 1-41 are pending.

Specification

1. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The claims are not drawn to the binary BAC vector itself but rather to methods using the vector and products comprising the vector.

Claim Objections

2. Claims 5 and 19 are objected to because of the following informalities:

In claim 5, step b), there is an unnecessary comma after the word "vector".

In claim 19, line 2 the phrase "unique restriction endonclease" lacks an adjective, such as "said".

Appropriate correction is required.

Claim R jections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-41 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 5, 29 and 34 are vague and indefinite in reciting "heterologous DNA". It is unclear with respect to what the DNA is heterologous: the non-plant host cell, an E. coli host cell or an Agrobacterium host cell?

Claim 17 is vague and indefinite in reciting "border sequences are derived from TL-DNA". The specification does not teach what the nature and number of derivative steps thus the metes and bounds of this claim cannot be ascertained.

Claim 19 recites the limitation "said selection marker" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 21 recites the limitation "said selection marker" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 24 recites the limitation "said selection marker" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 24 is vague and indefinite in reciting "selection is located adjacent to". In terms of a vector, the meaning of adjacent is not clear. Does this refer to 10 nucleotides? 100 nucleotides? Is "adjacent" relative to the overall size of the vector? The metes and bounds of the claim cannot be ascertained.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 19, 21 and 24 have been examined assuming their dependency should be to claims 18, 20 and 23 respectively, as such a dependency provides antecedant basis for the phrase "said selection marker".

7. Claims 1, 5-7, 11 and 13-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Hamilton (Gene (1997) 200: 107-116).

Hamilton 1997 teaches generating pCH20 vector which comprises Ri, a single copy origin of replication for Agrobacterium, the F origin of replication (single copy in E. coli), the conjugal origin of transfer oriT from RK2, left and right Agrobacterium T-DNA border sequences (from octopine plasmid TiA6), and a number of unique restriction sites between the left and right border sequences. This vector was then used to make BIBAC by inserting a DNA fragment comprising a fusion of GUS (β-glucuronidase, an E. coli gene) and NPTII (neomycin phosphotransferase II, originally cloned from transposon Tn5 in E. coli K12; confers resistance to kanamycin) was cloned into a unique SrfI site by the left border sequence. As a man-made fusion, this DNA fragment is heterologous with respect to any cell, including any bacterial cell, into which it is introduced. BIBAC2 contains a further selection marker, HYG, the hygromycin

resistance gene. Both the NPTII and the HYG genes are located between the left and right border sequences. The desired BIBAC vector was cloned and identified using standard molecular biology techiques, i.e. by transforming a ligation mixture into E. coli DH10B cells (non-plant host cells) and selecting kanamycin resistant cells. Absent evidence to the contrary it is assumed that the kanamycin resistance indicates the transformants express the heterologous NPTII DNA inserted into pCH20. pCH20, BIBAC and BIBAC2 all comprise the positive selection marker, sacB, which comprises a unique BamHI site; introduction of DNA into this BamHI site inactivates sacB. See entire document, especially p. 108, Sections 2.4 and 2.5, pp. 109-112, Sections 3.2 and 3.3, and Figures 1-3.

8. Claims 1, 5-7, 11 and 13-28 are rejected under 35 U.S.C. §102(b) as being anticipated by Hamilton et al (Plant Journal (1999) 18:223-229; cited in IDS).

Hamilton et al 1999 teach the use of a vector, BIBAC2, in constructing a tomato DNA genomic library. The details about what BIBAC2 comprises are discussed above; these features are inherent to the vector. Hamilton et al 1999 teach transforming E. coli DH10B cells (i.e. non-plant host cells) with a ligation mixture comprising BamHI-but BIBAC2 and size-selected tomato genomic DNA. Transformants were selected by kanamycin resistance and survival in 5% sucrose, indicating the sacB gene was inactivated by insertion of heterologous DNA into the BamHI site. See entire document, especially pp. 224-225.

Claim R jections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §§102(e), (f) or (g) prior art under 35 U.S.C. §103(a).

11. Claims 1, 5-8, 10, 11 and 13-29, 31 34 and 39 are rejected under 35 U.S.C. §103(a) as being unpatentable over Hamilton 1997 in view of Hamilton (USP 5,733,744).

Hamilton 1997 is applied as above to claims 1, 5-7, 11 and 13-28. Hamilton 1997 does not teach teach a method of introducing heterologous DNA into a non-plant host cell that is a mammalian cell, a non-plant eukaryotic cell containing a BIBAC vector or a method of isolating a DNA using a BIBAC vector and introducing the vector into a mammalian cell.

Hamilton '744 teaches the advantages of BIBAC vectors for transformations. BAC vectors are better for librarires as they are easier to construct, screen and maintain compared to YAC libraries (col. 2, lines 44-46). Specific for BIBAC vectors, the single copy plasmid origins of replication enable the stable maintenace of high molecular weight DNA in E. coli and A. tumefaciens (co. 4, lines 19-22). Use of BIBAC vectors for genomic libraries is taught (col. 5, lines 9-25). The vectors may be used for transient or stable transformation (col. 7, lines 43-44).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to use the BIBAC vector to transform/transfect mammalian cells to express large DNA inserts and to obtain DNA encoding the desired expression product. One of ordinary skill in the art would have been motivated to do so in order to take advantage of the stable maintenance of large DNA inserts in E. coli and Agrobacterium possible with the BIBAC vector, as well as the possibility of Agrobacterium-mediated transformation of other host cells (plant, yeast or filamentous fungi) without the labor and time involved in subcloning inserts into a different vector. As one of ordinary skill in the art appreciates, the capacity to maintain and transfer large inserts is ideal for eukaryotic genomes which typically comprise genes of large size.

12. Claims 1-9, 11-15, 17-30, 32-38, 40 and 41 are rejected under 35 U.S.C. §103(a) as being unpatentable over Hamilton 1997 in view of Hamilton (USP 5,733,744), de Groot et al (Nature Biotechnology (1998) 16:839-842) and Bundock et al (EMBO Journal (1995) 14:3206-3214).

Hamilton 1997 is applied as above to claims 1, 5-7, 11 and 13-28. Hamilton 1997 teaches that the design of the BIBAC vectro was intended to minimize its size and maximize its stability, and can comprise high-molecular-weight DNA inserts. See p. 109 under Section 3.2 and p. 113 under Section 3.8. Hamilton 1997 does not teach a method of introducing heterologous DNA into a non-plant host cell that is a yeast cell, a filamentous fungi cell, Saccharomyces cervisiae, Kluyveromyces lactis or Aspergillus, a non-plant eukaryotic cell that is a yeast cell containing a BIBAC vector or a method of isolating a DNA using a BIBAC vector and introducing the vector into a non-plant host cell that is a yeast cell.

Hamilton '744 teaches the advantages of BIBAC vectors for transformations. BAC vectors are better for librarires as they are easier to construct, screen and maintain compared to YAC libraries (col. 2, lines 44-46). Specific for BIBAC vectors, the single copy plasmid origins of replication enable the stable maintenace of high molecular weight DNA in E. coli and A. tumefaciens (co. 4, lines 19-22). Use of BIBAC vectors for genomic libraries is taught (col. 5, lines 9-25). The vectors may be used for transient or stable transformation (col. 7, lines 43-44). Transformation using BIBAC is not limited Agrobacterium but includes any method known in the art including eletroporation, calcium chloride and particle bombardment (col. 5, lines 24-26).

deGroot teaches Agrobacterium-mediated transformation of filamentous fungi, including Aspergillus niger and teaches that this means of transformation permits the transfer of intact high molelar weight DNA into fungal chromosomes. See entire document, especially p. 841 under Discussion.

Bundock et al teach Agrobacterium-mediated transformation of the yeast, Saccharomyces cerevisiae. See entire document.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to use a BIBAC vector to introduce heterologous DNA inserts into yeast or filamentous fungi and thereby obtain a non-plant eukaryotic host cell containing a BIBAC vector. It would also have been obvious to obtain heterologous DNA from with prokaryotic or eukaryotic genomes for use in such methods. It would also have been obvious to isolate a DNA encoding a desired gene product using a BIBAC vector and a non-plant eukaryotic host cell, such as yeast. One of ordinary skill in the art would have been motivated to do so because it was known that introducing DNA via Agrobacterium-mediated transformation was possible in these organisms and the BIBAC vector is ideal for cloning and transferring large DNA inserts as it was specifically designed to stably maintain large inserts in both E. coli and Agrobacterium strains. As one of ordinary skill in the art appreciates, the capacity to maintain and transfer large inserts is ideal for eukaryotic genomes which typically comprise genes of large size and is also ideal for prokaryotic organisms for cloning gene clusters or pathways. Consequently, such a vector lends itself to use in cloning by expression in, for instance, yeast cells since it enables one to test larger DNA inserts and encompass a greater variety in the inserts to be screened, as well as increase the possibility of cloning intact genes or gene clusters, rather than fragments.

Conclusion

Claims 1-41 are rejected.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from 11:00 AM to 7:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than the next business day after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, can be reached on (703) 305-1998.

The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Bronwen M. Loeb, Ph.D.
Patent Examiner
Art Unit 1636

March 23, 2003

JAMES KETTER
PRIMARY EXAMINER